

Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1-2. (Cancelled)

3. (Currently Amended) A process for fragmenting and labeling at least one synthetic or natural DNA, RNA or chimeric DNA-RNA polymer, comprising the steps of: chemically fragmenting ~~said member~~ the at least one DNA, RNA or chimeric DNA-RNA polymer in the presence of at least one multivalent metal cation in an aqueous solution, to produce a plurality of DNA or RNA fragments having freed terminal phosphates for further reaction; and

attaching a labeling agent on a plurality of said fragments at freed terminal phosphates located at the 3' end and/or 5' end of said fragments, wherein the fragmenting and attaching steps take place in an *in vitro* nucleic acid amplification mixture.

4-15. (Cancelled)

16. (Previously Presented) A process for fragmenting and labeling a synthetic or natural DNA or RNA nucleic acid, comprising the steps of:

chemically fragmenting said nucleic acid in the presence of at least one multivalent metal cation in an aqueous solution, to produce a plurality of DNA or RNA fragments having freed terminal phosphates for further reaction;

attaching a labeling agent on a plurality of said fragments at freed terminal phosphates located at the 3' end and/or 5' end of said fragments; and

treating said aqueous solution to decrease or eliminate unattached labeling agent, wherein the treating step physically separates the labeled nucleic acid fragment from unattached labeling agent in the aqueous solution after the fragmenting and attaching steps, and wherein the treating step dilutes an *in vitro* nucleic acid amplification mixture.

17-39. (Cancelled)

40. (New) The process according to claim 3, further comprising a treating step that physically separates labeled nucleic acid fragments from unattached labeling agent after the fragmenting and attaching steps.

41. (New) The process according to claim 40, wherein the treating step uses an organic solvent to separate the labeled nucleic acid fragment from the unattached labeling agent.

42. (New) The process according to claim 40, wherein the treating step separates a labeled nucleic acid fragment from unattached labeling agent by using solid phase extraction of the labeled nucleic acid fragment on a solid support.

43. (New) The process according to claim 40, wherein the treating step precipitates a labeled nucleic acid fragment at ambient temperature from the mixture that further contains betaine, dodecyl trimethylammonium bromide (DTAB) and unlabeled nucleic acid.

44. (New) The process according to claim 3, wherein the fragmenting and attaching steps are effected in separate steps.

45. (New) The process according to claim 3, wherein the DNA, RNA, or chimeric DNA-RNA polymer comprises at least one thiophosphate nucleotide.

46. (New) The process according to claim 45, wherein the fragmenting step for RNA or chimeric DNA-RNA polymer comprising at least one thiophosphate nucleotide is performed in the presence of at least one multivalent metal cation selected from the group consisting of Sr^{2+} , Ba^{2+} , Pb^{2+} , Cd^{2+} , Fe^{2+} , Ni^{2+} , Ru^{3+} , Ce^{3+} , Eu^{3+} , Tb^{3+} , Tm^{3+} , Yb^{3+} and Lu^{3+} and a chemical catalyst.

47. (New) The process according to claim 45, wherein the fragmenting step for RNA or chimeric DNA-RNA polymer comprising at least one thiophosphate nucleotide is

performed in the presence of at least one multivalent metal cation selected from the group consisting of Cr^{3+} , Ce^{3+} , Yb^{3+} , Tb^{3+} , Eu^{2+} and Pb^{2+} .

48. (New) The process according to claim 45, wherein the fragmenting step for RNA or chimeric DNA-RNA polymer comprising at least one thiophosphate nucleotide is performed in the presence of at least one multivalent metal cation selected from the group consisting of Be^{2+} , Cr^{3+} , Pb^{2+} , In^{3+} , Tb^{3+} , Ce^{3+} , Yb^{3+} and Ni^{2+} .

49. (New) The process according to claim 3, wherein the attaching step attaches a label to an internal or terminal thiophosphate nucleotide.

50. (New) The process according to claim 3, wherein the fragmenting step further includes use of a chemical catalyst.

51. (New) The process according to claim 50, wherein the chemical catalyst is selected from the group consisting of imidazole, a substituted analogue of imidazole and a compound that includes an imidazole ring or a substituted analogue of an imidazole ring.

52. (New) The process according to claim 50, wherein the chemical catalyst is selected from the group consisting of N-methylimidazole, 3-(N-morpholino) propane sulfonic acid (MOPS), N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES), piperazine-N,N'-bis (2-ethane sulfonic acid) (PIPES) and bioorganic polyamines.

53. (New) The process according to claim 3, wherein the fragmenting step for RNA or chimeric DNA-RNA polymer is performed in the presence of at least one multivalent metal cation selected from the group consisting of Sr^{2+} , Ba^{2+} , Pb^{2+} , Cd^{2+} , Fe^{2+} , Ni^{2+} , Ru^{3+} , Ce^{3+} , Eu^{3+} , Tb^{3+} , Tm^{3+} , Yb^{3+} and Lu^{3+} and a chemical catalyst.

54. (New) The process according to claim 3, wherein the fragmenting step for RNA or chimeric DNA-RNA polymer is performed in the presence of at least one multivalent metal cation selected from the group consisting of Cr^{3+} , Ce^{3+} , Yb^{3+} , Tb^{3+} , Eu^{2+} and Pb^{2+} .

55. (New) The process according to claim 3, wherein the fragmenting step for DNA or chimeric DNA-RNA polymer is performed in the presence of Tb^{3+} and a chemical catalyst.

56. (New) The process according to claim 3, wherein the fragmenting step for DNA or chimeric DNA-RNA polymer is performed in the presence of at least one multivalent metal cation selected from the group consisting of Be^{2+} , Cr^{3+} , Pb^{2+} , In^{3+} , Tb^{3+} , Ce^{3+} , Yb^{3+} and Ni^{2+} .

57. (New) The process according to claim 3, wherein the multivalent metal cation is selected from the group consisting of Tb^{3+} and Ce^{3+} .

58. (New) The process according to claim 3, wherein the mixture contains the labeling agent in a concentration of from 0.1 mM to 4 mM.

59. (New) The process according to claim 58, wherein the mixture contains the labeling agent in a concentration of from 0.1 mM to 1 mM.

60. (New) The process according to claim 58, wherein the mixture contains the labeling agent in a concentration of from 0.3 mM to 0.55 mM.

61. (New) The process according to claim 3, wherein the labeling agent contains alkyl halide or haloacetamide reactive functions.

62. (New) The process according to claim 3, wherein the labeling agent is selected from the group consisting of 5-(bromomethyl)fluorescein, 6-(bromomethyl)fluorescein, 6-iodoacetamidofluorescein and 5-iodoacetamidofluorescein.

63. (New) The process according to claim 16, wherein the treating step further includes adding an acid to the aqueous solution after the fragmenting and attaching steps.

64. (New) The process according to claim 16, wherein the treating step uses an organic solvent to separate the labeled nucleic acid fragment from the unattached labeling agent.

65. (New) The process according to claim 64, wherein the organic solvent is selected from the group consisting of 1-butanol, 2-butanol, isopentyl alcohol, 1-pentanol and cyclohexanol.

66. (New) The process according to claim 16, wherein the treating step separates a labeled nucleic acid fragment from unattached labeling agent by using solid phase extraction of the labeled nucleic acid fragment on a solid support.

67. (New) The process according to claim 66, wherein said solid support is selected from the group consisting of beads, gels, ion exchange resin, reverse phase resin, silica matrix and a membrane.

68. (New) The process according to claim 66, wherein the labeled nucleic acid fragment is eluted from the solid support by using a buffer containing betaine.

69. (New) The process according to claim 16, wherein the treating step precipitates the labeled nucleic acid fragment at ambient temperature from the aqueous solution that further contains betaine, dodecyl trimethylammonium bromide (DTAB) and unlabeled nucleic acid.

70. (New) The process according to claim 16, wherein the treating step comprises adding a quencher to the aqueous solution after the fragmenting and attaching steps.

71. (New) The process according to claim 70, wherein the quencher is selected from the group consisting of pyrophosphate, thiol derivative, chelating agent, phosphate anion and carbonate anion.

72. (New) The process according to claim 16, wherein the fragmenting and attaching steps are effected in separate steps.

73. (New) The process according to claim 16, wherein the DNA or RNA nucleic acid comprises at least one thiophosphate nucleotide.

74. (New) The process according to claim 73, wherein the RNA nucleic acid comprising at least one thiophosphate nucleotide is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Sr^{2+} , Ba^{2+} , Pb^{2+} , Cd^{2+} , Fe^{2+} , Ni^{2+} , Ru^{3+} , Ce^{3+} , Eu^{3+} , Tb^{3+} , Tm^{3+} , Yb^{3+} and Lu^{3+} and a chemical catalyst.

75. (New) The process according to claim 73, wherein the RNA nucleic acid comprising at least one thiophosphate nucleotide is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Cr^{3+} , Ce^{3+} , Yb^{3+} , Tb^{3+} , Eu^{2+} and Pb^{2+} .

76. (New) The process according to claim 73, wherein the DNA nucleic acid comprising at least one thiophosphate nucleotide is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Be^{2+} , Cr^{3+} , Pb^{2+} , In^{3+} , Tb^{3+} , Ce^{3+} , Yb^{3+} and Ni^{2+} .

77. (New) The process according to claim 16, wherein the RNA nucleic acid is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Sr^{2+} , Ba^{2+} , Pb^{2+} , Cd^{2+} , Fe^{2+} , Ni^{2+} , Ru^{3+} , Ce^{3+} , Eu^{3+} , Tb^{3+} , Tm^{3+} , Yb^{3+} and Lu^{3+} and a chemical catalyst.

78. (New) The process according to claim 16, wherein the RNA nucleic acid is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Cr^{3+} , Ce^{3+} , Yb^{3+} , Tb^{3+} , Eu^{2+} and Pb^{2+} .

79. (New) The process according to claim 16, wherein the DNA nucleic acid is chemically fragmented in the presence of Tb^{3+} and a chemical catalyst.

80. (New) The process according to claim 16, wherein the DNA nucleic acid is chemically fragmented in the presence of at least one multivalent metal cation selected from the group consisting of Be^{2+} , Cr^{3+} , Pb^{2+} , In^{3+} , Tb^{3+} , Ce^{3+} , Yb^{3+} and Ni^{2+} .

81. (New) The process according to claim 16, wherein the multivalent metal cation is selected from the group consisting of Tb^{3+} and Ce^{3+} .

82. (New) The process according to claim 16, wherein the aqueous solution contains the labeling agent in a concentration of from 0.1 mM to 4 mM.

83. (New) The process according to claim 82, wherein the aqueous solution contains the labeling agent in a concentration of from 0.1 mM to 1 mM.

84. (New) The process according to claim 82, wherein the aqueous solution contains the labeling agent in a concentration of from 0.3 mM to 0.55 mM.

85. (New) The process according to claim 16, wherein the labeling agent contains alkyl halide or haloacetamide reactive functions.

86. (New) The process according to claim 16, wherein the labeling agent is selected from the group consisting of 5-(bromomethyl)fluoroscein, 6-(bromomethyl)fluorescein, 6-iodoacetamidofluorescein and 5-iodoacetamidofluorescein.